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FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			SITTON, JEHANNE SOUAYA	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/025,137

Applicant(s)

LIU ET AL.

Examiner

Jehanne Souaya Sitton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 27-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12/01.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Claims 27-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant timely traversed the restriction requirement in the paper filed 6/24/2003.

2. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.

See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re*

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Brouwer and 35 U.S.C. § 103(b),” 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

3. An action on the merits of claims 1-26 follows.

Specification

4. The sequence listing filed 4/9/2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the sequence listing adds SEQ ID NOS 1 and 2, which were not present in the specification as filed. It is noted that the specification teaches that SEQ ID NOS: 1 and 2 are located 3' of N1 and N2 respectively, and references accession number AP002562 (see page 3), however accession numbers in Genbank can be changed, thus introducing the possibility of new matter into the specification. This objection can be overcome by providing the specific region of the Accession number (81889-83238) as a separate sequence in the sequence listing as well as a statement that the specific sequence was the version used from the accession number at the time of filing of the application. A section referring to the specific nucleotides of the accession number that were relied on for SEQ ID NOS 1 and 2 should also be included. It is also noted that such sequence of the accession number is considered essential material as sequences in the claims are dependent from the larger sequence.

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Accordingly, applicant is required to correct the new matter in the reply to this Office Action. (it is noted that claims reciting such SEQ ID NOS have been rejected under 112/first paragraph, but that such rejection will be overcome if a reply as outlined by the examiner above is provided in reply to this office action).

Claim Objections

5. Claims 9 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims recite primers that "contain" a specific sequence. Such language has no upper length limitation with regard to the primer, however, the claim from which these sequences depended recite an upper length limitation for the primers. Therefore, claims 9 and 12 are broader than claim 8.

Claim Rejections - 35 USC § 112

First Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, and 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

The sequence listing filed 4/9/2002 added SEQ ID NOS 1 and 2, which were not present in the specification as filed. It is noted that the specification teaches that SEQ ID NOS: 1 and 2 are located 3' of N1 and N2 respectively, and references accession number AP002562 (see page 3), however accession numbers in Genbank can be changed, thus introducing the possibility of new matter into the claims. This rejection can be overcome by providing the specific region of the Accession number (81889-83238) as a separate sequence in the sequence listing as well as a statement that the specific sequence was the version used from the accession number at the time of filing of the application.

8. Claims 1-3, 5-6, and 8-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims reciting nucleic acid sets (claims 1-3 and 5-6), nucleic acids obtained from amplification (claims 8-14) and claims to probes (claims 15-18) encompass mutants variants and homologs, as well as sequences from other species, that have not been taught or described by the specification. All of the claims referenced herein recite language that is sufficiently "open" such that the claims encompass unspecified sequences on either side of the recited SEQ ID NOS. Such nucleic acids therefore encompass a large genus of sequences that have not been disclosed or described by the specification. The single sequence of Accession number AP002562 does not

Objet (Shigella flexneri 2a str.301) : 9155 aatacataacagaaacctgaaacacaa 9129

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

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whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the recited SEQ ID NOS, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

Indefinite

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite primers that contain a specific SEQ ID NO (SEQ ID NO: 1-4); but the claims also recite that the primer can be a minimum of 18 nucleotides in length. The term “containing” stipulates that the full sequence is present in the larger sequence, however SEQ ID NOS: 3 and 4 are each 24 nucleotides in length. Consequently, it is unclear how a sequence can “contain” either SEQ ID NO: 3 or 4 and be 18 nucleotides long. Further, the claims recite probes that contain a specific SEQ ID NO: (SEQ ID NOS: 5-8) but also recite that the probe can be a minimum of 26 nucleotides. The term “containing” stipulates that the full sequence is present in the larger sequence, however SEQ ID NOS 5-7 are each 27 nucleotides in length. Consequently, it is unclear how a sequence can “contain” either SEQ ID NO: 5, 6, or 7 and be 26 nucleotides long.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession number AF175847 (November 2000).

Accession number AF175847 teaches a sequence that contains a sequence complementary to SEQ ID NO: 5 as shown below. The sequence of accession number is 161 nucleotides long. It is noted that the recitation of "sequences complementary thereto" has been broadly interpreted to encompass sequences complementary to portions of SEQ ID NO: 5, as the recitation does not limit the claim to sequences that contain the complete complement of SEQ ID NO: 5.

Qy	7	TAACAGAAACCTGAAACA	24
Db	24	TAACAGAAACCTGAAACA	7

13. Claims 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession number AX002476 (March 2000).

Accession number AX002476 teaches a sequence that contains a sequence complementary to SEQ ID NO: 6 as shown below. The sequence of accession number is 20 nucleotides long. It is noted that the recitation of "sequences complementary thereto" has been broadly interpreted to encompass sequences complementary to portions of SEQ ID NO: 6, as the recitation does not limit the claim to sequences that contain the complete complement of SEQ ID NO: 6.

Qy	11	TTCCTGCGATTTC	23
Db	17	TTCCTGCGATTTC	5

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-3, 5-6, 8-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession number AE005490 (first appeared in Genbank on 1/25/2003), Genbank Accession number AE000346 (December 1, 2000), Genbank accession number Z70523 (April 1996) and Genbank accession number D90887 (1997) in view of Buck et al (Referred to as Buck: Biotechniques, vol. 27, pp 528-536, 1999), Hammond et al (Referred to as Hammond; US Patent 5,374,718), Hogan (US Patent 5,693,469) and Tijhie et al (Referred to as Tijhie; J. Microbiol. Meth. Vol. 18, pp 137-150, 1993).

Accession number AE005490 teaches a gene sequence from the E. coli genome at positions. The accession number specifically teaches that the encoded proteins for genes from positions 1933-3282 are 100% identical to E. coli K 12. Accession numbers AE000346 (December 1, 2000), Z70523 (April 1996) and D90887 also teach sequences from different strains of E. coli. The positions of each of SEQ ID NOS 1-8 within these accession numbers are provided. The accession numbers do not teach the sequences of SEQ ID NOS 1-8, however,

Hammond teaches and exemplifies a method for picking probes for detection of a particular organism (in the case of Hammond it was for *Chlamydia pneumoniae*) that are species specific (see abstract). Hammond teaches that probes are chosen upon alignment of different sequences of a particular region and that genus specific and species specific probes can be chosen based on the alignment of the sequences to target regions of similarity or differences (see col. 2, lines 49-60, and cols 4-8). Hogan teaches targeting sequences within the *E. coli* genome for detection of *E. coli*. Tijhie teaches a method of picking probes and primers for genus and species detection of *Chlamydia*. Tijhie teaches using computer assisted sequences analysis of known sequences to identify regions of similarity and differences to construct genus and species specific probes and primers (see abstract, fig. 1, pages 141-142). Buck teaches design strategies for choosing DNA primers. Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that *every single primer* worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, *every single control primer* functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however

different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to construct probes and primers for the purpose of detecting *E. coli*. The ordinary artisan would have been motivated to do so given the teachings of Hogan that nucleic acid based methods could be used to detect *E. coli*. Given that a large number of *E. coli* genomic sequences containing SEQ ID NOS 1-8 were known (see Accession numbers cited above) the ordinary artisan would have been motivated to use such sequences to detect *E. coli* in view of the large amount of teaching in the prior art as to how to pick probes and primers for the detection of a target organism when target sequences were known (see Hammond, Hogan, Tijhie, and Buck). The claims encompass a genus of nucleic acid sequences which the ordinary artisan would have been motivated to construct for the purpose of detecting *E. coli*. Given the known *E. coli* sequences and the large amount of direction given in the prior art, the ordinary artisan would have been motivated to construct a genus of primers and probes for detection of *E. coli*. The ordinary artisan would have been motivated to target this particular region of *E. coli* because Accession Number AE005490 teaches that this region is conserved in *E. coli*. Further, given the teachings of Hammond and Tijhie, the ordinary artisan would also have observed that this region of *E. coli* was conserved upon aligning the available genomic sequences of *E. coli* and would have been motivated to target this conserved region for the purpose of constructing probes and primers to detect *E. coli*. The genus of probes and primers that the skilled artisan would be motivated to construct given the teachings of the prior art are considered equivalent for the

purpose of detecting E. coli to the genus of claimed probes and primers, absent secondary consideration. The claims encompass a fairly large genus and the ordinary artisan would have motivated to generate a genus of equivalent probes and primers for the purpose of detecting E.coli, therefore the genus of sequences encompassed by the claims obvious over the cited art. The state of the art was very high at the time the invention was filed with regard to picking primers and probes from already known sequences for the purpose of detecting the sequences as exemplified by the teachings of Buck, Hogan, Hammond, and Tijhie.

It is noted that the instant rejection has not been applied to claims 4, 7, and 19-26. As exemplified by the specification, such specific sequences exhibited unexpected results in that they were capable of detecting E. coli and not a large number of other genus and species of bacteria, including certain strains of Shigella, which is known in the art to be closely related to E. coli. As such, claims directed to the scope of the unexpected results (that is the specific SEQ ID NOS) are allowable over the cited prior art. However, the remaining claims are broader in scope and are not directed to any specific sequence, but rather to a large genus of sequences. (Further, addition of sequences on either side of SEQ ID NOS 1-8 would be expected to change the hybridization specificity of the resulting sequences as compared to those exemplified by the specification.) Since an extremely large amount of prior art was available at the time the invention was filed with regard to picking probes and primers to already known sequences (the larger sequence from which the genus of sequences containing or comprising the recited SEQ ID NOS was known) for the purposes of detecting those sequences, the genus of sequences encompassed by the claims is obvious over the teachings of the prior art. While picking the *specific* sequences of nucleic acid molecules consisting of any one of SEQ ID NOS 1-8 is not

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obvious as the prior art does not lead the ordinary artisan to pick the specific sequences consisting of SEQ ID NOS: 1-8, the claims are not directed to specific sequences but to a large genus of sequences which the prior art does provide motivation to construct for the purposes of detecting the large sequence from which the genus is derived. Further, the teachings of the prior art provide a reasonable expectation of success that such genus of sequences will be able to be used as probes and primers for detection of certain strains of *E. coli*.

Conclusion

17. Claims 4, 7, and 19-26 are free of the cited prior art.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

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Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne (Souaya) Sitton

Primary Examiner

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Jehanne Sitton
12/29/03